In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-1869V
Filed: August 12, 2024

STEPHANE FIORELLO and ANTHONY FIORELLO, on behalf of their minor child, R.F.,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Andrew Donald Downing, Downing, Allison, & Jorgenson, Phoenix, AZ, for petitioner
Ryan Pohlman Miller, U.S. Department of Justice, Washington, DC, for respondent

Decision[1]

On December 4, 2017, petitioners filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),[2] alleging that a hepatitis B vaccination that their minor child, R.F., received on December 4, 2014, caused him to develop systemic inflammatory response syndrome ("SIRS"). (ECF No. 1; ECF No. 29, ¶¶ 32-33.) For the reasons set forth below, I conclude that petitioners are *not* entitled to an award of compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In

[1] Because this document contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the document will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] Within this decision, all citation to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. § 300aa-11(c).

In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A)-(B); § 300aa-11(c)(1)(C)(i); § 300aa-14(a). In this case, petitioners' allegations do not implicate any Table Injury.

When the vaccine recipient suffered an injury *not* of the type covered in the Vaccine Injury Table, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines ex rel. Sevier v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). In this case, petitioners must meet this burden of proof for establishing causation-in-fact.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279-80; *Hines*, 940 F.2d at 1525. Under that standard, the petitioners must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioners need not show that the vaccination was the sole cause but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioners must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" with the logical sequence being supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *see also Grant ex rel. Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting a causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

II. Procedural History

This case was initially assigned to another special master. (ECF No. 4.) It was reassigned to the undersigned on August 29, 2019. (ECF No. 43.)

Because this case was filed close to the expiration of the statute of limitations, the allegations of the initial petition were limited to contending that R.F. had suffered a severe adverse reaction to his vaccination. (ECF No. 1.) Petitioners filed a statement by Ms. Fiorello (Ex. 1) and medical records (Exs. 2-17) between December of 2017 and April of 2018. (ECF Nos. 8-11, 13-14, 16, 18.)

Respondent filed his Rule 4 Report on August 6, 2018. (ECF No. 24.) Respondent contended that the medical records did not satisfy petitioner's burden of proof with respect to proving that R.F. suffered a severe adverse reaction to his vaccination. (*Id*. at 12.) Petitioners subsequently filed R.F.'s school records (Exs. 19-20), additional medical records (Ex. 21), and an amended petition more specifically alleging that R.F. suffered SIRS. (ECF No. 28; ECF No. 29, ¶¶ 32-33; ECF No. 30.)

On August 27, 2019, petitioners filed an expert report by internist and infectious disease specialist Ravi Durvasula, M.D. (ECF No. 41; Exs. 22-23; *see also* ECF No. 45; Exhibits 24-26 (supporting literature).) Respondent filed a responsive expert report by pediatrician and infectious disease specialist Hayley Gans, M.D., on December 20, 2019. (ECF No. 46; Exs. A-B.) Petitioners then filed a further report by Dr. Durvasula in March of 2020. (ECF No. 49; Ex. 27.)

Thereafter, an entitlement hearing was set to be held in December of 2021. (ECF No. 54-55.) However, in the process of preparing for the hearing, the parties determined that they preferred to resolve the case on the written record. (ECF No. 59.) During a status conference held October 28, 2021, I advised the parties that I was amenable to resolving the case on the written record, but that I required further clarification from the experts regarding the nature of the conditions at issue, specifically hypersensitivities, SIRS, and chronic immune dysregulation. (*Id*. at 1-2.)

Petitioners then filed updated medical records (Exs. 28-29) in December of 2021 and a supplemental report by Dr. Durvasula (Ex. 30) in July of 2022. (ECF Nos. 60, 67.) Respondent filed a supplemental report by Dr. Gans in January of 2023. (ECF No. 71; Ex. C.)

Petitioners filed their brief regarding entitlement and further updated medical records on April 11, 2023. (ECF Nos 75-76; Ex. 31.) R.F.'s updated medical records revealed that he had undergone genetic testing and respondent requested an opportunity to review those results. (ECF No. 78.) Petitioner filed a final set of medical records on July 17, 2023. (ECF No. 79; Ex. 32.) Respondent filed his response to petitioners' brief regarding entitlement on August 8, 2023. (ECF No. 81.) Petitioners filed their reply brief on August 21, 2023. (ECF No. 82.)

This matter is now ripe for resolution. I have concluded that the parties have had a full and fair opportunity to develop the record and that it is appropriate to resolve this case without an entitlement hearing. *See Kreizenbeck ex rel. C.J.K. v. Sec'y of Health & Human Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020) (citing *Simanski v. Sec'y of Health & Human Servs*., 671 F.3d 1368, 1385 (Fed. Cir. 2012)); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2).

III. Factual History

a. Medical Records

R.F. is a triplet, who was born prematurely by cesarian section at 29 weeks of gestation. (Ex. 14, pp. 13-14.) His Apgar scores were eight at one minute and eight at five minutes. (*Id.* at 13.) While in the NICU, he was treated for respiratory distress syndrome, hyperbilirubinemia, choroid plexus cyst, retinopathy of prematurity, apnea, tachycardia, and feeding difficulties. (*Id.*)

At his 12-month well visit, mild to moderate speech delay and feeding difficulties were noted. (Ex. 17, pp. 7-9.) By his two-year well visit, he was receiving regular speech therapy and received a recommendation for occupational therapy to assist with sensory integration difficulties. (*Id.* at 13-15.) By the time of his three-year well visit, R.F. displayed delays in his gross motor skills and was referred to physical therapy. (*Id.* at 22-24.) At his five-year well visit, a neurodevelopmental evaluation was recommended due to his sensory issues, behavioral problems, fine and gross motor issues, and speech delays. (Ex. 5, pp. 6-10.) Following that evaluation, R.F. was

diagnosed with fine and gross motor delays, a sensory processing disorder, Attention Deficit Hyperactivity Disorder ("ADHD"), constipation, and mild anxiety. (Ex. 17, pp. 52-57.)

On August 28, 2014, R.F. received his first hepatitis B vaccination. (Ex. 5, p. 11.) He returned for his second hepatitis B vaccination, which is the subject of this petition, on December 4, 2014. (*Id.* at 14.) The second hepatitis B dose was delayed because R.F. had an upper respiratory infection in October of 2014. (*Id.* at 12-13; Ex. 1, ¶ 17.) Prior to administration of the December 4, 2014 hepatitis B vaccine, R.F.'s medical records express no concern regarding any immunologic condition or abnormality. Petitioners' brief discusses petitioners' observation that R.F.'s two triplet sisters faced greater struggles with common childhood illnesses than did R.F. (ECF No. 76, pp. 2-4.) However, this was a comparative observation with no indication that either R.F.'s or his sisters' immune responses were abnormal. Petitioners' brief also discusses an unusual sudden onset of colorblindness occurring in the autumn of 2014, as well as eye pain and other issues with R.F.'s vision. (*Id.* at 4-17.) While there are some references in the later medical records questioning whether R.F.'s eye problems were related to his hepatitis B vaccine (*see* Ex. 15, p. 1; Ex. 4, pp. 4-9; Ex. 28, p. 30), petitioners have not argued that this is a part of R.F.'s alleged vaccine injury. R.F. was eventually tested for optic neuritis, but the etiology of his vision complaints remained "unclear." (Ex. 15, pp. 1-3.) The course of R.F.'s medical encounters for his vision problems are not summarized. R.F. also suffered a fracture of his right wrist on November 19, 2014. (Ex. 10, pp. 2-5.) The follow up encounters for that fracture are also not summarized.

The day after vaccination, on December 5, 2014, R.F. presented to urgent care with pallor and an altered mental state ("intermittently becomes obtunded[3]"), though he was noted to be oriented to time, place, and person. (Ex. 3, pp. 2-3.) The onset was acute and occurred after he had been picked up from school. (*Id*. at 2.) There was no history of trauma or ingestion and no fever, vomiting, or headache. (*Id*.) Petitioners reported a family history of "severe vaccine reactions" and that R.F.'s grandfather had recently been hospitalized with a staph infection. (*Id*. at 3.) It was also later reported that R.F. had been treated for an upper respiratory infection with a full course of antibiotics just a week early. (Ex. 11, p. 4.) Petitioners also reported R.F.'s "recent cough and [upper respiratory infection symptoms]," to R.F.'s emergency room physicians. (Ex. 5, p. 23.) However, no additional medical records have been filed that reflect this presentation and treatment. Physical exam was otherwise normal.[4] (Ex. 3, p. 2.) Bloodwork revealed elevated ALP, AST, glucose, and white blood cell count, as

[3] "Obtund" refers to a reduced level of sensation or alertness. *Obtund*, DOLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=34619&searchterm=obtund (last visited July 15, 2024).

[4] In her statement, Ms. Fiorello indicates that R.F.'s temperature was taken repeatedly and confirmed hypothermia measured at 94ºF. (Ex. 1, ¶ 21.) However, this is not reflected in the medical record. R.F.'s initial vitals included a temperature of 96.7ºF and hypothermia is not noted. (Ex. 3, p. 2.) During subsequent transport to the hospital, R.F. was observed to be "warm, dry, pale in color." (Ex. 11, p. 4.)

well as low creatinine. (*Id.* at 3-4.) R.F. was placed on a saline IV and was transferred via EMS to a pediatric emergency department. (*Id*. at 4; *see also* Ex. 11, pp. 2-6.)

Upon arrival at the emergency department, R.F. was seen immediately due to a high probability of life threatening deterioration. (Ex. 11, p. 12.) He was placed on a cardiac monitor and an ECG was obtained. (*Id.*) IV fluids were administered, and additional lab work was ordered, which showed some improvement in leukocytosis. (*Id.*) Pediatric neurology was consulted. (*Id.*) There was low suspicion for seizures, but an EEG and further neurology follow up was recommended. (*Id.*) The initial impression was "unresponsive episode" with a differential diagnosis including syncope, seizure, or intercurrent illness. (*Id*.) R.F. was discharged home the same day. (*Id*.)

About three months later, on March 6, 2015, R.F. was seen by his pediatrician for symptoms of an upper respiratory infection. (Ex. 5, pp. 17-19.) It was reported that R.F. had experienced an episode wherein he "turned pale yesterday & skin was cold. Mom thought he was going to faint." (*Id*. at 17.) He experienced a hypotonic episode of about 30 minutes with no loss of consciousness, after which he was lethargic and drowsy. (*Id.*) He was back to normal after about three hours. (*Id*.) It was further reported that R.F. had a "similar episode 6 weeks ago after Hep B vac. [S]aw neuro who thought it was from the vac. [N]euro report not in EMR."[5] (*Id*.) Physical exam was normal except for nasal congestion. (*Id*.) R.F. was diagnosed with an unspecified upper respiratory infection and a "hypotonic/hyporesponsive episode." (*Id*. at 18.) Further follow up was recommended to rule out any seizure disorder or other neurologic problem. (*Id.*) An EEG was subsequently performed on March 27, 2015, and was overall normal. (Ex. 9, p. 95.) That record indicates that, in addition to two episodes of near passing out, R.F. also had a history of migraines. (*Id*.)

R.F. had his annual exam on March 25, 2015, at which time additional immunizations, including a further dose of hepatitis B, was recommended.[6] (Ex. 5, pp. 20-22.) R.F. was then evaluated by an allergy and immunology specialist, John J. Oppenheimer, M.D. on April 2, 2015, because "[t]here is concern with regard to next vaccination and direction is needed." (Ex. 2, p. 2.) The assessment was as follows:

> Status post episode of hypotonia with systemic complaints following vaccination to hepatitis B. Certainly, it is easy to blame the hepatitis vaccine for this; however, mechanistically, this is by no means an allergic response. Thus, skin testing will not aid. This certainly appears to be potentially an

[5] Although the emergency department record notes that neurology was consulted, I have not located any separate neurology consultation record. The emergency department record is limited to noting that the neurologist "did not feel his symptoms or the story was consistent with a seizure." (Ex. 11, p. 12.) In her statement, Ms. Fiorello indicates that the emergency department physician expressed of R.F.'s presentation that "it did appear this may be vaccine related in reviewing the events of the last 24 hours and the vaccine was the only thing out of the ordinary." (Ex. 1, ¶ 24.) However, she appears to indicate that her discussion with the neurologist was focused instead on a possible optic neuritis (*Id.* at ¶ 25), which was subsequently not indicated (Ex. 15, pp. 1-3).

[6] He also presented with ear pain. (Ex. 5, p. 20.)

> immune response and may speak to why three months later he had another episode when questionably it was a viral related illness. I am [aware] that neurology is following and I wholeheartedly encourage continued follow up as obviously the differential is protean. Presently, they are looking for potential seizures or migraines as etiology; however, it would be nice to know what potential triggers may bring this about for future observation.

(*Id.* at 3.)

On May 18, 2015, R.F. presented to another medical center for "other convulsions." (Ex. 9, p. 7.) The assessment indicated that R.F. was presenting with "episodes concerning for seizures" with pallor and limpness.[7] (*Id*. at 15.) In addition to the two episodes discussed above, the provided history also includes a discussion of episodes of "eye buggies" primarily in the right eye that last for a few seconds and are associated with watery eyes. (*Id.* at 12.) The records are inconsistent regarding the onset of the "eye buggies," with one history placing onset in March of 2015 (*Id*.) and another placing onset in August of 2014 (*Id*. at 16). In her statement, Ms. Fiorello explains: "over the first month of school, [R.F.] began complaining of 'eye bogies' where his eyes would suddenly tear and he would run from the room. He explained the light was hurting his eyes and making him cry." (Ex. 1, ¶ 15.) From May 18, 2015 to May 20, 2015, R.F. was hospitalized and underwent a 48-hour video EEG observing him while both awake and asleep. (Ex. 9, pp. 31-32.) During this period, he experienced multiple episodes of "bugs in the eyes" and no EEG changes were seen. (*Id*. at 31.) The EEG was interpreted as normal and the observed episodes deemed nonepileptic. (*Id*. at 31-32.)

R.F. presented with a cough and fever on May 25, 2017. (Ex. 28, pp. 28-31.) It was reported that R.F. "goes into shock with every new virus, one episode on Saturday." (*Id.* at 28.) These episodes were classified as "immune episodes," and it was noted that these episodes "[s]eem[ed] to have started after starting Hep B series." (*Id.* at 29-30.) R.F. was assessed with a fever, with no signs of a bacterial infection, and "hypotensive episode[s]" with "unclear etiology." (*Id.* at 31.) On July 19, 2017, R.F. established care with Jeffery Siegel, M.D. (Ex. 6, p. 31.) Dr. Siegel explained that he had reviewed R.F.'s medical records and that R.F. suffered reactions to viral infections that started after he received both hepatitis B vaccines. (*Id.* at 31-32.) Dr. Siegel reported that R.F.'s episodes involved "pallor, hypotension, decreased mental status." (*Id.* at 31.) Dr. Siegel reported that R.F. had been evaluated by an immunologist who reported that R.F.'s condition was not an allergic or anaphylactic reaction, but is, instead, an immune reaction. (*Id.* at 32.) Dr. Siegel assessed petitioner with an "[i]mmune hypersensitivity reaction by mechanism." (*Id.*)

[7] The records from this medical center indicate that R.F.'s episodes included a loss of consciousness (Ex. 9, p. 31) whereas the prior records indicated altered mental status without indicating a loss of consciousness (Ex. 3, pp. 2-3 (obtunded but oriented to time, place, and person) and Ex. 5, p. 17 (specifying no loss of consciousness)).

On August 17, 2017, R.F. was evaluated by S. Reed Shimamoto, M.D. for "immune deficiency." (Ex. 4, p. 4.) Dr. Shimamoto reported that R.F. was born 29 weeks premature and had an "prolonged NICU stay." (*Id.*) He explained that after R.F. received his first hepatitis B vaccine, "he went color blind had seen ophthalmology for eye disease." (*Id.*) Dr. Shimamoto then reported that, 23 hours after R.F.'s second Hep B vaccine, "he had symptoms of septic shock" and a decrease in his white blood cell count. (*Id.*) Dr. Shimamoto explained that R.F. has continued to suffer from these episodes following viral infections. (*Id.* at 4-5.) He describes R.F.'s episodes as "one quick cough, like a cat clearing its throat and then within 60 seconds he has complete pallor, non-responsive, floppy, [and] his body temperature drops to 96 [degrees]." (*Id.* at 5.) Dr. Shimamoto expresses "concern about possible relationship to vaccinations and these episodes," however, he was unable to offer a definitive diagnosis. (*Id.* at 6.) He then ordered "an immune screen" and recommended reviewing R.F.'s "vaccine responses from his infant series to see if there is a pattern of specific immune related disease." (*Id.*) R.F. broke his arm again in October of 2017 and was subsequently diagnosed with osteopenia. (*See* Ex. 7, pp. 23-26; Ex. 29, pp. 48-53.)

On April 27, 2018, R.F. saw Michael Daines, M.D., and allergy and immunology fellow Pamela Tongchinsub, M.D., for an "evaluation of suspected vaccination reaction, after developing fever, leukocytosis, and a range of episodic sins and symptoms including gagging reflux, cough, body temperature drops, turns pale, lips turn white, tachycardic." (Ex. 21, p. 3.) Dr. Tongchinsub noted "these symptoms appear without occurrence of vaccines as well." (*Id.*) She reported that R.F.'s differential diagnosis included POTS, mastcell, congenital heart disease, and idiopathic anaphylaxis. (*Id.*) She explains that R.F.'s condition was unlikely "immunodeficiency or vaccine reaction." (*Id.*) Mast cell was eventually ruled out in August of 2018. (*Id.* at 12.)

R.F. underwent genetic testing on April 12, 2021, which was normal. (Ex. 32, pp. 35-67.) R.F. was evaluated by cardiologist Theresa Grebe, M.D., on April 21, 2021. (*Id.* at 20-23.) After summarizing R.F.'s symptoms and completing an exam, Dr. Grebe reported that she "can not think of any clear unifying etiology that would explain [R.F.'s] symptoms," and she explained that she did not think any cardiology follow up was necessary. (*Id.* at 22.) R.F. had a wellness check on August 18, 2021 with Dr. Siegel. (Ex. 31, p. 10-13.) He was assessed with "immune hypersensitivity reaction by mechanism," under which Dr. Siegel reported that his work up remained negative. (*Id.* at 13.)

b. Declaration

Petitioner, Stephane Fiorello, filed a statement in this case. (Ex. 1.) Petitioner explained that her son R.F. is a triplet and was born premature on December 8, 2008. (*Id.* at ¶ 3.) R.F. was transferred to the NICU and his "course was unremarkable beyond the common issues of prematurity, which included retinopathy of prematurity, respiratory distress syndrome, apnea, tachycardia, and feeding difficulties." (*Id.* at ¶ 4.) R.F. was also diagnosed "with an uncomplicated, unsealed gluteal cleft and a choroid plexus cyst that resolved shortly after birth." (*Id.*)

While in the NICU, R.F. received the RSV vaccine. (Ex. 1, ¶ 5.) The rest of R.F.'s vaccinations were initially postponed until his expected due date in February of 2009, where thereafter, R.F. began the typical vaccine schedule for newborns, except petitioner declined hepatitis vaccines. (*Id.*) In mid-January, R.F. transitioned out of the NICU and was able to go home. (*Id.* at ¶ 6.) However, he continued to be monitored by the NICU and he experienced "gross motor delays, speech delays, and sensory processing issues," which, petitioner testified, was "typical of prematurely born children." (*Id.* at ¶ 7.) R.F. made improvements in these areas and "was a very happy, very affectionate child," however, he did experience stress and anxiety when leaving the house. (*Id.* at ¶ 8.) Petitioner also testified that R.F. "generally had a higher resistance to most viruses rarely suffering more than typical childhood symptoms of nasal/sinus congestion and to a much lesser duration than what [petitioners] saw with his sisters." (*Id.* at ¶ 11.)

Petitioners were required "to administer the Hep B vaccine prior to school entry," and R.F. received the vaccine at his pediatrician's office. (Ex. 1, ¶¶ 12, 14.) After receiving the first vaccine, petitioner testified that R.F. developed colorblindness. (*Id.* at ¶16.) R.F.'s second Hep B vaccination was delayed due to illness, however, he eventually received it on December 4, 2014. (*Id.* at ¶ 18.) After his appointment, R.F. "was very tired and had little appetite," however, petitioner felt this was normal, given R.F.'s anxiety. (*Id.*) The next day, while driving R.F. and his siblings home from school, petitioner noticed that R.F. had developed a chocking cough. (*Id.* at ¶ 19.) When petitioner got her children home and out of the car, she turned around to find R.F. standing by the car, "completely pale," and, when they eventually got him inside, his legs buckled. (*Id.* at ¶¶ 19-20.) Petitioner took R.F. to urgent care after his condition did not improve. (*Id.* at ¶ 20.)

By the time petitioner and R.F. made it to urgent care, R.F. "was showing cognitive deficits and appeared to be losing consciousness." (Ex. 1, ¶ 21.) R.F. was hypotensive and hypothermic and his bloodwork showed that he had a blood infection, and his WBC was elevated. (*Id.* at ¶¶ 21-22.) R.F. was taken by ambulance to the hospital, and he was given IV antibiotics. (*Id.* at ¶ 24.) Petitioner explained that the only thing out of the ordinary that R.F. had been exposed to was the vaccine. (*Id.*) Petitioner goes on to summarize R.F.'s medical history, which is summarized, in detail, above. (*Id.* at ¶¶ 26-37.)

Petitioner testified that, since December of 2014, R.F. has had between six and seven hypotensive and hypothermic episodes per year. (Ex. 1, ¶ 37.) Petitioner testified that R.F.'s subsequent episodes have been triggered by viral infections, instead of vaccinations. (*Id.*) Petitioner testified that R.F.'s condition has significantly impacted their lives. (*Id.* at ¶ 38.) Petitioner specifically described two episodes after R.F. had a respiratory infection in July of 2017. (*Id.* at ¶ 39.) Petitioner testified that R.F. "does have immunity to all previously administered vaccines which is comforting considering he is still medically exempt from further vaccination in the continued absence of a diagnosis." (*Id.* at ¶ 40.) In October of 2017, R.F. was diagnosed with osteopenia after

breaking his wrist. (*Id.* at ¶ 41.) Petitioner testified that this was surprising because, before receiving his second hepatitis B vaccination, R.F. had broken his arm, and had no signs of osteopenia. (*Id.*)

Petitioner explains that R.F. does not have an official diagnosis, therefore, "all that is known is that it began with a Hep B vaccine, but by what mechanism is unclear." (Ex. 1, ¶ 42.) Due to his condition, petitioners are "hyper vigilant to R.F.'s condition." (*Id.* at ¶ 43.) R.F. "is at high risk for falls and possible serious injury," and "heart complications and loss of oxygen to critical organs." (*Id.*) Additionally, R.F. has had to undergo invasive diagnostic methods that have posed additional complications for R.F. due to his ADD and Sensory Processing Disorder. (*Id.* at ¶ 44.) Petitioner testified that "R.F.'s complaints referenced above and those contained in his medical records were caused-in-fact by the Hepatitis B vaccination received on December 4, 2014." (*Id.* at ¶ 45.)

IV. Expert Opinions

a. Petitioner's expert, Ravi Durvasula, M.D.[8]

After reviewing R.F.'s history, Dr. Durvasula opined that his "health took a very different course following his hepatitis B vaccines." (Ex. 22, p. 4.) Dr. Durvasula explained that prior to vaccination, R.F. had "no particular immune deficiency, disease vulnerability[,] or developmental disorder." (*Id*.) He opines that R.F.'s prematurity at birth and resulting complications cannot explain his immunologic picture. (*Id*. at 5.) After his second hepatitis B vaccination, however, he suffered an "initial reaction characterized by leukocytosis, hypothermia and hypotonia" that Dr. Durvasula opines constituted "a clear systemic inflammatory response to vaccination." (*Id*. at 4.) Thereafter, R.F. continued to experience subsequent episodes "all presumably triggered by viral illnesses" and with "[n]o clear association between these episodes and additional vaccines." (*Id*.) Because etiologies such as bacterial sepsis, seizures, or cardiovascular disease were excluded, Dr. Durvasula concludes an exaggerated immune response to vaccination was "the most likely cause." (*Id*.) Further to this, Dr. Durvasula stresses that R.F. was ultimately found to suffer osteopenia post-vaccination, which is very abnormal for a child and is associated with chronic immunologic disease. (*Id*. at 5 (citing Rainer H. Straub et al., *Evolutionary Medicine and Bone Loss in Chronic Inflammatory Diseases – A Theory of Inflammation-Related Osteopenia,* 45 SEMINARS ARTHRITIS & RHEUMATISM 220 (2015) (Ex. 24)).) Thus, he opines that the exaggerated response to vaccination is the cause of R.F.'s ongoing immune system dysregulation and resulting recurrent sepsis-like episodes. (*Id*.)

[8] Dr. Ravi Durvasula received both a bachelor's in biology and his medical degree from McGill University. (Ex. 23, p. 1.) He completed a residency in internal medicine at Baylor College of Medicine and a fellowship at Yale University School of Medicine in infectious diseases. (*Id.* at 3.) Dr. Durvasula currently works as the Chairman of the Department of Medicine and the John W. Clark Endowed Professor of Medicine in the Department of Public Health Sciences at Loyola University Stritch School of Medicine. (*Id.* at 1.) He has published 75 peer reviewed manuscripts, over 90 peer reviewed abstracts and conference proceedings, and five books. (*Id.* at 5-14.)

Dr. Durvasula suggests his opinion is in agreement with two treating physicians who opined that R.F. had suffered a "hyperimmune reaction" as distinct from an allergic reaction (immunologist Dr. Oppenheimer) or an "immune hypersensitivity reaction" (primary care provider Dr. Siegel). (Ex. 22, p. 4 (citing Ex. 2, pp. 2-3; Ex. 6, p. 32).) Dr. Durvasula acknowledges that this is a "very rare complication" for which there is no specific test that could prove the connection to the vaccination. (*Id.*) However, he indicates that "the link between the vaccine, subsequent viral challenges and a severely exaggerated immune cascade resembling shock is plausible." (*Id*.) He indicates that "[a]ctivation of the immune system, the very basis of vaccines, can become dysregulated and several triggers – medications, autoimmune signals and infectious pathogens – play etiologic roles." (*Id*.) He suggests that "[t]hermal regulation, hemodynamic stability and level of arousal may all be correlated with immune-reactive molecules" and that "[s]uch highly exaggerated responses have been reported in the literature and abnormal profiles of immunity, though rare, are described." (*Id*. at 4-5 (citing L. Beretta et al., *Churg-Strauss Vasculitis with Brain Involvement Following Hepatitis B Vaccination,* 19 CLINICAL & EXPERIMENTAL RHEUMATOLOGY 757 (2001) (Ex. 25); Nancy Agmon-Levin et al., *Vaccines and Autoimmunity,* 5 NATURE REVS. RHEUMATOLOGY 648 (2009) (Ex. 26)).)

Dr. Durvasula disagrees with Dr. Gans's opinion on respondent's behalf that R.F. suffered a chronic pre-existing immune condition. (Ex. 27, p. 1.) He stresses that there is a clear association between the onset of R.F.'s symptoms and his hepatitis B vaccination. (*Id.*) Thus, especially because Dr. Gans does not identify a specific condition, he charges that "[t]here is no causal evidence for this argument and it is simply a refusal to acknowledge the prospect of vaccine-induced hyperimmune responses without offering an etiology." (*Id*.) Dr. Durvasula also disagrees that R.F.'s condition can be explained as Postural Orthostatic Tachycardia Syndrome ("POTS"). (*Id.*) Although POTS was included in at least one differential diagnosis, R.F.'s medical evaluations were inadequate to support such a diagnosis and his clinical history does not indicate that his condition is postural, which is the core basis for diagnosing POTS. (*Id*.) Whereas Dr. Gans stresses a lack of biologic data to support a causal link to vaccination, Dr. Durvasula counters that "this case relies on clinical data and physicians' records. The biologic basis of such reactions I not part of clinical evaluation and absence of such data should not be used to dismiss this claim." (*Id*. at 1-2.)

b. Respondent's expert, Haley Gans, M.D.[9]

[9] Dr. Hayley Gans received a bachelor's in biochemistry from Connecticut College and her medical degree from SUNY Health Science Center at Syracuse. (Ex. B, p. 1.) She completed an internship and residency program in the Department of Pediatrics and a fellowship in the Division of Pediatric Infectious Diseases at Stanford University School of Medicine. (*Id.*) Dr. Gans currently works as a clinical professor and Director of Fellowship Education in the Department of Pediatrics, and the Fellowship Associate Program Director of Pediatrics Infectious Diseases at Stanford University Medical Center. (*Id.*) Dr. Gans published 30 peer review articles, nine book chapters, and 34 abstracts. (*Id.* at 5-10.)

Based on her review of R.F.'s medical history, Dr. Gans concludes that R.F. has suffered an unnamed condition without any known specific etiology. (Ex. A, p. 4.) She acknowledges that the frequent episodes associated with infectious triggers, history of allergic tendencies, and family history of autoimmunity has led to a working diagnosis of self-limited "allergic-like" responses; however, she stresses that R.F.'s condition is chronic and lacks a single inciting event. (*Id*.) She notes that the hepatitis B vaccine has been associated with anaphylaxis, but not chronic conditions. (*Id*. at 5 (citing Kathleen R. Stratton, et al., *Summary of a Report from the Institute of Medicine,* 271 J. AM. MED. ASS'N 1602 (1994) (Ex. A, Tab 5); Julie Mouchet et al., *Hepatitis B Vaccination and the Putative Risk of Central Demyelinating Diseases – A Systematic Review and Meta-Analysis,* 36 VACCINE 1548 (2018) (Ex. A, Tab 6)).) She further notes that a seizure disorder has not been entirely ruled out and that an alternative working diagnosis of POTS has also been proposed. (*Id*. at 4-5.) Although Dr. Gans appears to acknowledge that a POTS diagnosis has not been made in this case, she opines that it is a good fit for his clinical history of episodic lightheadedness, brain fog, and exaggerated heart rate, as well as his family history of autoimmunity. (*Id*. at 5.)

Dr. Gans agrees that it may have initially been reasonable to investigate whether R.F.'s December 2014 event was a response to his vaccination; however, "this is not a reasonable assumption over time when the events are recurrent and occur after a heterogenous group of inciting events." (Ex. A, p. 5.) According to Dr. Gans, "what is clear is that over time, as R.F. has experienced more episodes and more evaluations have occurred, his treating physicians have begun to understand R.F.'s chronic condition better." (Ex. C, p. 1.) She continues

> Over time the allergy/immunology physician, using all of the clinical and laboratory information, concluded that R.F. did not have anaphylaxis, SIRS and hyperimmune response and that the Hepatitis B vaccine that had initially been a consideration given the temporal relationship to the first episode was not the "cause" of the recurrent episodes; that these recurrent episodes would occur with many different triggers.

(*Id*. (citing Ex. 2, pp. 2-10; Ex. 4, pp. 1-9; Ex. 21, pp. 1-3).)

Dr. Gans charges that Dr. Durvasula's opinion lacks any evidence beyond temporality to implicate R.F.'s vaccination as an inciting trigger. (Ex. C, p. 1.) Further, Dr. Gans disagrees with the characterization of R.F.'s condition as "sepsis-like." (*Id.* at 2.) She explains that neither a sepsis-like condition nor a SIRS would self-resolve in hours. (*Id*. at 2-3; Ex. A, p. 5.) SIRS in particular is not a recurrent condition.[10] (Ex. C, p. 3.) Dr. Gans also challenges Dr. Durvusla's reliance on a hyperimmune response. She indicates no biologically plausible explanation has been offered to explain how a

[10] Quoting the International Consensus Statement on Pediatric Sepsis (not filed), Dr. Gans characterizes SIRS as "when a child has an abnormality of temperature (fever of hypothermia) or age-specific abnormality of the white blood cell count and one of the following: tachycardia, bradycardia, respiratory distress, or pulmonary condition requiring mechanical ventilation," which she opines is "clearly" not consistent with R.F.'s presentation. (Ex. C, p. 3.)

hyperimmune response to vaccination would lead to later hyperimmune responses to subsequent unrelated infectious exposures. (Ex. A, p. 5.) Dr. Gans explains that

> The biologic process in hypersensitivity is an abnormal reaction to a *specific antigen* which occurs in one of two ways, from either preformed IgE antibodies to a specific protein or antigen (which is the immediate form) or from T-Cells also to a specific protein or antigen (which is the delayed form). The hypersensitivity reaction occurs only to the specific protein or antigen, and only recurs upon re-exposure to *this particular* antigen, not unrelated antigens.

(Ex. C, pp. 2-3 (emphasis original).)

Dr. Gans contends that Dr. Durvasula's reliance on publications by Staub, et al., Beretta, et al., and Agmon-Levin, et al., are inapposite as they involve different conditions and the reactions discussed in those publications do not fit R.F.'s history. (Ex. A, pp. 5-6 (citing Straub et al., *supra,* at Ex. 24; Beretta et al., *supra,* at Ex. 25; Agmon-Levin et al., *supra,* at Ex. 26).) To the extent Dr. Durvasula invokes triggers of autoimmune disease, he has not identified any autoimmune disorder as being at issue. (Ex. C, p. 3.)

In her second report, Dr. Gans further questions whether R.F.'s episodes are actually associated with viral illnesses, which would point away from an immunologic basis for the condition. (Ex. C, p. 2.) Dr. Gans opines that "R.F. has an underlying condition, the cause of which is likely genetic, with manifestations after variable triggers. These triggers do cause the clinical signs and symptoms but do not cause the underlying condition." (*Id*. at 3.) Thus, while the vaccination may have been temporal to the first episode, the condition otherwise operates independently of the vaccination. (*Id*. at 3-4.)

V. Party Contentions

a. Petitioners' motion

Petitioners explain that their theory under *Althen* prong one is based on their assertion that "R.F. suffered a systemic inflammatory response syndrome reaction to vaccination." (ECF No. 76, p. 31.) They contend that, although no conclusive diagnostic test is available, "the link between the vaccine, subsequent viral challenges and a severely exaggerated immune cascade resembling shock is likely." (*Id*. at 32.) In support of this position, petitioners cite at turns Dr. Durvasula's explanation of hypersensitivity reactions and literature addressing triggers of autoimmunity. (*E.g., id*.) They further stress the proposed mechanism of action included in the Beretta, et al., case report of Churg-Strauss vasculitis following the hepatitis B vaccine, which involves proinflammatory cytokines recruiting mononuclear cells to lead to local tissue damage. (*Id*. at 33 (citing Beretta et al., *supra,* at Ex. 25).) According to petitioners', the article by

Straub, et al., additionally shows that bone loss is associated with immune inflammation. (*Id*. at 34-35 (discussing Straub et al., *supra,* at Ex. 24).)

Regarding *Althen* prong two, petitioners stress that prior to his hepatitis B vaccines, there is no evidence that R.F. was suffering any immune disorder; however, his health took a very different course subsequent to vaccination. (ECF No. 76, pp. 35-36.) Thus, Dr. Durvasula opines that "there is a clear association between onset of R.F.'s symptom complex and hepatitis B vaccination." (*Id*. at 35 (quoting Ex. 27, p. 1).) Further to this, petitioners argue that two of R.F.'s treating physicians, Drs. Oppenheimer and Siegel, reached the same conclusion as Dr. Durvasula – that R.F. experienced a hyperimmune reaction. (*Id*. at 36.) Moreover, the fact that R.F. has been diagnosed with osteopenia at age 9 supports immune dysregulation and chronic inflammation as the process underlying R.F.'s clinical syndrome. (*Id*. at 36-37.) Petitioners contend that their proposed explanation of events is more likely than the idea that onset of R.F.'s condition was merely coincident to vaccination. (*Id*. at 37.)

Regarding *Althen* prong three, petitioners argue that onset of R.F.'s syndrome in the form of an acute reaction one day post-vaccination constitutes an appropriate temporal relationship. (ECF No. 76, p. 37.) Indeed, they urge that "temporality following vaccination is a major piece of the clinical picture." (*Id*.) However, petitioners do not actually explain the temporal relationship in their brief.

Regarding respondent's ability to identify any factor unrelated to vaccination as the cause of R.F.'s condition, petitioners stress that respondent has not explained any alternative cause. (ECF No. 76, pp. 38-39.) To the extent Dr. Gans invoked POTS, petitioners dispute that R.F. can reasonably be diagnosed with POTS. (*Id.* at 37.)

b. Respondent's response

As a threshold issue, respondent contends that an *Althen* analysis is not even necessary, because petitioners have failed to demonstrate that R.F. suffered either SIRS or any hypersensitivity reaction as alleged. (ECF No. 81, p. 23.) While respondent acknowledges that Dr. Gans could not otherwise identify R.F.'s condition, he stresses that SIRS and/or a hypersensitivity reaction cannot explain R.F.'s chronic, recurrent condition. (*Id*. at 23-25.)

Regarding *Althen* prong one, respondent contends that petitioners have not demonstrated any sound and reliable medically theory supporting the hepatitis B vaccine as a cause of R.F.'s claimed injuries. (ECF No. 81, p. 25.) Respondent contends that, while the hepatitis B vaccine can cause anaphylaxis, it is not known to cause any chronic condition and Dr. Durvasula himself characterized his theory of immune dysregulation as entirely unsupported by diagnostic testing and instead based on merely "plausible" association, which does not meet petitioners' preponderant burden of proof. (*Id.* at 26-27 (quoting Ex. 22, p. 5).) R.F. does not have any of the autoimmune conditions discussed in the literature cited by Dr. Durvasula. (*Id*. at 27.) Respondent also challenges the relevance of the relationship between chronic

inflammatory diseases and osteopenia, because R.F. had only episodic reactions to stimuli rather than any chronic inflammatory disease. (*Id*. at 28.)

Regarding *Althen* prong two, respondent stresses that just prior to the vaccination at issue R.F. had also recently suffered an upper respiratory infection. (ECF No. 81, p. 29 (citing Ex. 5, p. 12; Ex. 11, pp. 2-5).) He acknowledges that the treating physicians noted the temporal proximity of R.F.'s first episode to vaccination but contends this does not support petitioners' claim for two reasons. (*Id*. at 30.) First, considering R.F.'s medical history as a whole, later medical records expressed doubt that the vaccination was implicated after the subsequent episodes occurred. (*Id*. (citing Ex. 21, p. 3).) Second, the records of Drs. Oppenheimer and Siegel cited by petitioners are more equivocal regarding vaccine causation than petitioners suggest. (*Id*. at 30-32.) Further, respondent contends that Dr. Siegel did not reach an independent assessment of R.F.'s initial episode, but merely documented the prior assessments of the other treating physicians. (*Id*. at 32.) In any event, even if the treating physicians did opine in a manner supportive of petitioners' claim, these opinions must still be assessed for their reliability. (*Id*.) Petitioners' expert, Dr. Durvasula, provided no evidence, apart from temporality of the first episode, to support his hypothesis of a SIRS or hyperimmune response. (*Id*. at 34.) However, respondent stresses the importance of evaluating R.F.'s condition based the broader history of recurrent episodes. (*Id*. at 33.)

Regarding *Althen* prong three, respondent contends that "[i]t is impossible to know what an appropriate temporal association between vaccination and R.F.'s condition would be, as the condition is unknown, and the timeline is complicated by the recurrent, ongoing episodes in response to unknown causes." (ECF No. 81, p. 34.) Therefore, respondent contends that petitioners have not met their burden under *Althen* prong three.

c. Petitioners' reply

In reply, petitioners stress that their amended petition alleged SIRS and further explained that "[a]lthough his immediate systemic response eventually subsided, it left R.F. with a pronounced immune system dysregulation, such that a new immune system provocation leads to another, predictable event." (ECF No. 82, pp. 1-2 (quoting ECF No. 29, ¶ 32).) Petitioners further argue that R.F.'s initial episode meets the criteria for SIRS. (*Id*. at 2-3.) Therefore, petitioners contend that they have both pled and substantiated a specific injury. (*Id*. at 3-4.)

In response to respondent's *Althen* prong one arguments, petitioners dispute that the literature respondent has cited shows the hepatitis B vaccine to be considered safe. Petitioners stress that while vaccinations are safe at a population level, this does not preclude rare adverse events. (ECF No. 82, pp. 6-7.) Moreover, the publications cited by respondent are not conclusive. (*Id*. at 7.) Regarding respondent's urging that Dr. Durvasula lacks supporting clinical evidence, petitioners stress that what Dr. Durvasula acknowledged was that "testing for such a response is not in the realm of standard clinical care." (*Id.* at 7- 8 (quoting Ex. 22, p. 5).) Petitioners argue that they should not

be held to account for what testing is or is not available. (*Id*. at 8.) Petitioners indicate that it is a mischaracterization of Dr. Durvasula's opinion to suggest he opined based on mere plausibility and stress that they are not arguing that plausibility is their burden of proof. (*Id*. at 8-9.)

Regarding *Althen* prong two, petitioners disagree with respondent's assessment of Drs. Oppenheimer's and Siegal's opinions. (ECF No. 82, pp. 10-14.) Petitioners stress that it is not the role of treating physicians to flesh out a medical theory of causation, that the records include "incredibly powerful language supporting [a] vaccine reaction," and that picking apart the treaters' thought process creates an impossible burden for petitioners. (*Id.* at 14.) Petitioners charge that respondent's position amounts to asserting that any time a treating physician records an impression that does not support respondent's view, then that physician "must not have thought things through correctly." (*Id*. at 13-14.)

Regarding *Althen* prong three, petitioners cite a prior case in which respondent presented two experts who opined that the SIRS manifests immediately after a triggering event. (ECF No. 82, pp. 14-15 (citing *Ahlum v. Sec'y of Health & Human Servs*., No. 12-763V, 2018 WL 4323623, *44 (Fed. Cl. Spec. Mstr. Aug. 16, 2018).)

VI. Analysis

As discussed above, petitioner's burden in a cause-in-fact claim is to show the three-part *Althen* test, which includes (1) a general theory of causation implicating the vaccine as a cause of the alleged condition, (2) a logical sequence of cause and effect implicating the vaccination as a cause of petitioner's own condition, and (3) appropriate timing of onset based on the theory of causation, by a preponderance of evidence. 418 F.3d at 1278. In this case, the parties present issues with respect to all three *Althen* prongs.[11]

Importantly, petitioners' claim has two components. First, petitioners have confirmed in their briefing that they are asserting that R.F. experienced a hypersensitivity reaction to his hepatitis B vaccine that resulted in SIRS. Second, they also contend that, although the initial episode subsided, it resulted in "a pronounced immune system dysregulation, such that a new immune system provocation leads to another, predictable event." (ECF No. 82, p. 2 (quoting ECF No. 29, ¶ 32).) This latter assertion is crucial to petitioners' case.

[11] If one assumes that R.F. suffered a life-long immune disorder as respondent implicitly argues, then arguably this case should be evaluated under the *Loving* test for significant aggravation. *See Loving ex rel. Loving v. Secretary of Health & Human Servs.,* 86 Fed. Cl. 135 (2009). However, this approach was not discussed by either party. Petitioners, in particular, argue that R.F.'s condition arose *de novo* post vaccination. In any event, there is no debate between the parties that R.F.'s post-vaccination episode was the first clinical indication that he had any kind of immune disorder. Accordingly, any analysis under *Loving* prongs one through three would readily identify a worsening of R.F.'s condition occurring post-vaccination. The remaining elements of the *Loving* test would remain the same as the *Althen* analysis below. Thus, conceptualizing this case as one of significant aggravation would not change the outcome.

Because R.F.'s initial episode, allegedly a vaccine-caused hypersensitivity reaction resembling SIRS, did not in itself persist for at least six months and did not result in either death or surgical intervention, it does not standing alone meet the Vaccine Act's statutory severity requirement. § 300aa-11(c)(1)(D)(i). Therefore, petitioners only state a compensable claim if they can present a medical theory and logical sequence of cause and effect demonstrating not only that a hepatitis B vaccine can cause a hypersensitivity reaction, but also that R.F.'s alleged post-vaccination hypersensitivity reaction was in turn the cause of the alleged chronic immune system regulation they additionally assert as the second component of their claim.[12] *Wright ex rel. B.W. v. Sec'y of Health & Human Servs.*, 22 F.4th 999, 1005 (Fed. Cir. 2022) (holding that for purposes of § 300aa-11(c)(1)(C)(ii) a vaccine injury must be a substantial contributing factor and but for cause of any complications or residual effects under § 300aa-11(c)(1)(D)(i)).

a. *Althen* prong one

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.,* 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, although the theory need not be scientifically certain, "it must still be 'sound and reliable.'" *Boatmon ex rel. J.B. v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Knudsen*, 35 F.3d at 548-49).

According to Dr. Durvasula, what R.F. experienced was an "initial reaction characterized by leukocytosis hypothermia and hypotonia," which was later followed by subsequent similar episodes involving hypothermia, unresponsiveness, and hypotonia, each presumably triggered by viral illnesses. (Ex. 22, p. 4.) He further characterizes the initial episode as a hypersensitivity response and as SIRS. (*Id*. (explaining that the initial episode "closely resembled a picture of septic shock and is a clear systemic inflammatory response to vaccination" and expressing agreement with Dr. Siegel's diagnosis of hypersensitivity reaction.) Although Dr. Durvasula invokes SIRS as an

[12] R.F.'s ophthalmic condition may have separately persisted for greater than six months; however, despite raising the fact that R.F. began having vision problems subsequent to his first hepatitis B vaccine, petitioners have not incorporated that aspect of R.F.'s history into their theory. Dr. Durvasula opined that any relationship between R.F.'s first hepatitis B vaccine and his visual disturbances is "unclear." (Ex. 22, p. 3.) At no point did he incorporate R.F.'s ophthalmic issues into his assessment of R.F.'s allegedly vaccine-caused condition.

explanation for the features of R.F.'s initial clinical presentation, he is clear in basing his underlying causal theory on a hypersensitivity response.[13] (Ex. 30, p. 4.) He agrees that only the first episode was associated with vaccination.[14] (*Id*.) As Dr. Gans explains, however, hypersensitivity responses are antigen-specific. (Ex. C, pp. 2-3.) Accordingly, hypersensitivity alone does not explain R.F.'s episodic presentation given that the later episodes were triggered by other unspecified viral illnesses. Dr. Gans opines that "there is no biologic condition where one trigger, e.g. a vaccine, causes a 'normal' response to suddenly chronically dysregulate so that all subsequent unrelated exposures cause the same dysregulation." (Ex. C, p. 2.) Dr. Gans confirms that hypersensitivity reactions and SIRS are acute responses that do not present chronically and/or episodically. (*Id*. at 3.)

After being prompted to explain how a hypersensitivity reaction can be related to chronic immune dysregulation, Dr. Durvasula asserted that hypersensitivity "often has features of cross-reaction or molecular mimicry," which is an invocation of autoimmunity. (Ex. 30, p. 4; *see also* Ex. 22, p. 4 (indicating that "[a]ctivation of the immune system, the very basis of vaccines, can become dysregulated and several triggers – medications, autoimmune signals and infectious pathogens – play etiologic roles.")) To support that point, Dr. Durvasula relies on a paper by Agmon-Levin, et al., for the proposition that autoimmunity can arise in susceptible individuals as a result of environmental triggers, including from vaccine antigens that stimulate the innate and adaptive immune responses. (Ex. 30, p. 4 (quoting Agmon-Levin et al., *supra,* at Ex. 26, p. 2).) Apart from his citation to Agmon-Levin, Dr. Durvasula has not otherwise articulated how R.F.'s alleged post-vaccination hypersensitivity reaction could have led to the chronic state of immune dysregulation he posits.

Dr. Durvasula glosses over the details of the proposed relationship between hypersensitivity and autoimmunity. Indeed, Dr. Durvasula does not even clarify what type of hypersensitivity he is invoking. (*Compare* Ex. 30, p. 4 (invoking either immediate or delayed hypersensitivity) *and* Ex. C, p. 2 (explaining immediate and delayed hypersensitivity as involving different mechanisms).) For its part, the Agmon-Levin paper couches hypersensitivity and autoimmunity as two distinct concepts,

[13] Specifically, he explains that hypersensitivity reactions "result in widespread activation of the immune system resulting in both cellular and humeral derangements that manifest as hypersensitivity. These reactions may be immediate or delayed and manifestations can overlap with clinical features of Systemic Inflammatory Response Syndrome." (Ex. 30, p. 4.)

[14] Although Dr. Gans stresses in her first report that the hepatitis B vaccine is "safe and efficacious," that discussion is explicitly limited to "chronic conditions." (Ex. A, p. 5.) Dr. Gans suggests that Dr. Durvasula has not substantiated any causal relationship between R.F.'s hepatitis B vaccine and his condition and contends that his overall chronic, episodic condition is not consistent with either SIRS or a hypersensitivity reaction. (*Id.* at 4-5.) However, nowhere in either of her reports does she suggest that, as a general matter, a vaccine cannot cause these types of acute immune reactions. She acknowledges, for example, that the hepatitis B vaccine can cause anaphylaxis acutely. (*Id.* at 5.) In her second report, Dr. Gans appears to explain without any apparent qualification that any antigen has the potential to result in a hypersensitivity reaction. (*See* Ex. C, pp. 2-3.) Because this decision turns on other factors, I will simply assume without deciding that the hepatitis B vaccine can cause hypersensitivity reactions.

without discussing the former as a cause of the latter. (Agmon-Levin et al., *supra,* at Ex. 26.) But in any event, even if accepting that a vaccine could result in hypersensitivity leading to autoimmunity, Dr. Durvasula's ultimate reliance on autoimmunity in this case would still be unsupported *ipse dixit* that cannot be credited. There is no question that autoimmunity is an established category of disease that can, in at least some instances, be linked to vaccination. *See* 42 CFR § 100.3(b)(15). However, there are various pathways to autoimmunity and many autoimmune conditions have little to no suspicion of vaccine causation. *E.g. Kelly v. Sec'y of Health & Human Servs.,* No. 16-1548V, 2023 WL 3274159, at *19 (Fed. Cl. Spec. Mstr. May 5, 2023) (explaining that "[t]here is little debate that myasthenia gravis is an autoimmune neuromuscular disorder and there is little debate that molecular mimicry is, in general, a viable theory of autoimmunity that can in at least some contexts implicate vaccination. Importantly, however, these predicates are not enough to meet petitioner's burden of proof."); *Casazza v. Sec'y of Health & Human Servs.,* No. 17-947V, 2023 WL 6214984, at *10 (Fed. Cl. Spec. Mstr. Aug 30, 2023) (explaining "there is no dispute that [rheumatoid arthritis] is an autoimmune condition of uncertain cause" and that [v]ery little on this record apart from Dr. Gershwin's say-so associates any vaccine with [rheumatoid arthritis] whereas much more purports to refute Dr. Gershwin's opinion.") Despite invoking the concept as the sole explanation for the chronic immune dysregulation he posits, Dr. Durvasula has not substantiated that autoimmunity is relevant to this case and has not sufficiently articulated a theory based in autoimmunity.

Although Dr. Durvasula opines that R.F.'s presentation is suspicious for an autoimmune process, he has not purported to invoke any known autoimmune condition. Instead, Dr. Durvasula highlights two aspects of R.F.'s chronic condition as pertinent to his theory. First, he indicates that "[t]hermal regulation, hemodynamic stability and level or arousal may all be correlated with immune-reactive molecules." (Ex. 22, p. 4.) Second, he notes that diffuse osteopenia is associated with chronic immunologic disease. (*Id.* at 5.) However, he has not identified any autoimmune condition that could potentially explain these features as part of its clinical presentation. Nor has he otherwise identified any autoimmune pathway could theoretically result in such a presentation. As Dr. Gans has pointed out, R.F. does not have any of the various autoimmune conditions discussed in any of the literature cited by Dr. Durvasula. (Ex. A, p. 5; Ex. C, p. 3.) In fact, in reviewing R.F.'s history, Dr. Durvasula observes that "[e]xtensive immunologic and allergy testing failed to reveal a clear abnormality, immunosuppressive illness or associated disorder of cellular or humoral immunity." (Ex. 22, p. 3.)

The Beretta, et al., case report posits that pro-inflammatory cytokines may ultimately lead to recruitment of tissue damaging mononuclear and T cells; however, this hypothesis is presented in the context of vasculitis, which is explained as involving a process whereby the endothelial cells of the blood vessels in particular are affected. (Beretta et al., *supra,* at Ex. 25.) Again, however, there has been no assertion that R.F. suffered vasculitis or that vasculitis could explain R.F.'s clinical presentation. Nothing on this record substantiates that the mechanism of injury discussed within this case report can be reasonably generalized to other conditions or invoked to explain a

presentation such as in this case. For example, Dr. Durvasula has not even explained as a general matter his assertion that thermal regulation and hemodynamic stability are immune-mediated. And, in any event, the case report acknowledges that the hypothesized mechanism of vaccine-induced vasculitis is still a matter of debate. (*Id*.)

"Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case, although the explanation need only be 'legally probable, not medically or scientifically certain.'" *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1345 (Fed. Cir. 2010) (quoting *Knudsen*, 35 F.3d at 548-49).) In that regard, "[m]edical recognition of the injury claimed is critical and by definition a 'vaccine-related injury,' i.e. illness, disability, injury or condition, has to be more than just a symptom or manifestation of an unknown injury." *Id*. at 1349. Thus, without more, Dr. Durvasula's broad reliance on an unspecified autoimmune process fails on a fundamental level. Simply, it is too vague to preponderantly support a theory of causation. *Accord J.F. v. Sec'y of Health & Human Servs.*, No. 13-799V, 2022 WL 5434214, at *32 (Fed. Cl. Spec. Mstr. Sept. 9, 2022) (finding that "petitioner is not persuasive in identifying ASIA as a sound and reliable means of identifying the presence of an autoimmune injury in those who are not suffering a defined autoimmune condition. Given that petitioner did not suffer any recognized autoimmune condition, this is fatal to petitioner's *Althen* prong one showing.")

Dr. Durvasula does more specifically state that hypersensitivity can result in cross reaction and molecular mimicry, which is a known mechanism of autoimmunity. (Ex. 30, p. 4.) Molecular mimicry "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler,* 2020 WL 4593162, at *20 (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 18, 2019)). Even accounting for the fact that petitioners are not obligated to demonstrate scientific certainty, prior cases have expressed with regard to the application of molecular mimicry that "[t]he line must be drawn somewhere between speculation and certainty." *Brayboy v. Sec'y of Health & Human Servs.,* No. 15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021). Without requiring direct, testable evidence, this still generally requires some showing of cross-reactive potential affecting the health and productivity of a bodily tissue or organ. *Id*. Here, however, Dr. Durvasula merely references the possibility of cross-reaction. He does not identify any proposed homology, any relevant autoantibody, or even explain what specific autoimmune target within the body would be responsible for "[t]hermal regulation, hemodynamic stability and level or arousal." (Ex. 22, p. 4.)

Dr. Durvasula stresses that

> Though a variety of cellular assays could be done under laboratory conditions to elucidate the link between vaccine and environmental virus antigens and R.F.'s immune reactions, this case relies on clinical data and physicians' records. The biological basis of such reactions is not part of

> clinical evaluation and absence of such data should not be used to dismiss this claim.

(Ex. 27, pp. 1-2.) However, petitioners' burden under *Althen* prong one is to demonstrate general causation, which is not restricted to an examination of R.F.'s own history. Accordingly, the limits of R.F.'s own clinical evaluation are not a reason for Dr. Durvasula to entirely side-step any substantiation of the biological basis for his theory. Nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *aff'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013). The Court of Federal Claims has previously explained that, while the *Althen* Court rejected the need for scientific certainty, "[t]he standard of proof does not operate as a sliding scale that varies depending upon the quantity and quality of the scientific evidence that is available." *Caves v. Sec'y of Health & Human Servs*., 100 Fed. Cl. 119, 143 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012). Here, while the limits of clinical evaluation have some bearing on what evidence petitioners can reasonably be expected to muster relative to *Althen* prong two, such limitations cannot explain the dearth of evidence or explanation supporting Dr. Durvasula's opinion regarding general causation.

Considering all of the above, Dr. Durvasula's opinion does not preponderantly establish that the hepatitis B vaccine can cause a hypersensitivity reaction *that would in turn cause* chronic immune dysregulation resulting in episodic presentations of hypothermia, unresponsiveness, and hypotonia, coupled with diffuse osteopenia. Therefore, petitioners have not met their preponderant burden of proof with respect to *Althen* prong one.[15]

[15] I note that there is one prior Court of Federal Claims decision in which a special master was found to have erred because he effectively required the petitioner to "demonstrate causation for each recurring outbreak of a chronic condition triggered by a vaccine and that each recurrence must be separately analyzed under *Althen*." *DeLozier ex rel. L.T. v. Sec'y of Health & Human Servs*., 152 Fed. Cl. 558, 569 (2021). The instant case is distinguishable. In *DeLozier*, the special master concluded that petitioner had established that a child's vaccination did initially play a causal role in bringing about the autoimmune condition of alopecia, which was a condition known to have a chronic course that waxed and waned. *Id.* at 560. Having concluded that the vaccine played a role in initially causing the condition, the fact that the condition waxed and waned, consistent with the understood course of such a condition, was not a barrier to recovery for the entirely of the condition. *Id.* at 569. Here, however, the initial, allegedly vaccine-caused, episode, *might* be a part of a more chronic condition that would appear to present episodically; however, that condition remains unidentified and the relationship between the initial episode and the chronic condition is not clear. Moreover, regardless of the nature of that unidentified chronic condition, respondent and his expert further challenge that the type of immune reaction theorized by petitioners to explain the initial episode (hypersensitivity or SIRS) can reasonably be implicated as a cause of chronic immune dysregulation. Accordingly, what was taken for granted in *Delozier* – that all of the episodes were manifestations of the underlying condition that was itself vaccine-caused – is a core point of litigation in this case from which I have concluded that petitioners have not proven their case.

b. *Althen* prong two

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a vacinee's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326-27; *Grant*, 956 F.2d at 1147-48. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras ex rel. Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. *See* § 300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder,* 88 Fed. Cl. at 745 n. 67 ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted.") A petitioner may support a cause-in-fact claim through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.,* 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines,* 940 F.2d at 1528).

i. Treating physician opinions

In their briefing, petitioners stress the opinions of two treating physicians – Drs. Oppenheimer and Dr. Siegel.[16] (ECF No. 82, pp. 10-14.) According to petitioners, their records include "incredibly powerful language supporting [a] vaccine reaction." (*Id.* at 14.) While I agree that these records do state an impression of vaccine-causation vis-à-vis R.F.'s initial post-vaccination episode, I do not agree that they reliably support vaccine-causation of R.F.'s condition.

Turning first to Dr. Oppenheimer's earlier specialist evaluation of April 2, 2015, he offers two statements that support petitioners' view. First, addressing R.F.'s condition as "[s]tatus post episode of hypotonia with systemic complaints following vaccination to hepatitis B," he states that "[c]ertainly, it is easy to blame the hepatitis for this." (Ex. 2, p. 3.) Second, he explains that "[t]his certainly appears to be potentially an immune response and may speak to why three months later he had another episode when questionably it was a viral related illness." (*Id*.) Dr. Oppenheimer specifies that he does not believe the episode was an allergic response but does not otherwise characterize the type of immune response he is considering. Importantly, however, there are other aspects of Dr. Oppenheimer's record that are not supportive of

[16] In their reply, petitioner's also quote a record from Phoenix Children's Hospital as evidence that the medical records "continue to reflect vaccination involvement." (ECF No. 82, p. 9 (quoting Ex. 32, p. 20).) However, this record is not illuminating. The language petitioners' quote is from the history of present illness portion of a cardiology consultation, which the record specifies was obtained from petitioners themselves. (Ex. 32, p. 20.) It does not contain any medical opinion endorsing the reported history of a vaccine reaction and the cardiologist recorded that the case involved a "confusing clinical situation." (*Id*.) Ultimately the cardiologist's impression was that "I can not think of any clear unifying cardiac etiology that would explain his symptoms." (*Id*. at 22.)

petitioners' claim. First, Dr. Oppenheimer states that "I wholeheartedly encourage continued follow up as obviously the differential is protean." (*Id*.) Second, he states that "it would be nice to know what potential triggers may bring this about for future observation." (*Id*.)

Regarding R.F.'s initial post-vaccination presentation, although I agree that Dr. Oppenheimer's record includes an impression from a qualified specialist that R.F.'s initial episode was an immune reaction to the vaccine, it is not ultimately strong evidence. As respondent stresses, the fact that Dr. Oppenheimer is a treating physician is not the end of the discussion. (ECF No. 81, p. 32.) The reliability of his impression must be assessed. In that regard, although Dr. Oppenheimer indicates that it is "easy" to blame the initial episode on R.F.'s vaccination, there is reason to doubt the factual assumptions underlying that assessment. In particular, there is no indication that Dr. Oppenheimer was aware of the fact that R.F. had also been suffering an infection in the week prior to the episode. (*Compare* Ex. 2, p. 2 (Dr. Oppenheimer's April 2015 recorded history making no mention of any upper respiratory infection) *and* Ex. 5, p. 23 (December 5, 2014 ED triage noting recent URI symptoms) *and* Ex. 11, p. 4 (December 5, 2014 EMS record stating "Pt was treated for an upper respiratory infection last week, and has completed a full course of antibiotics."))[17] The omission of this aspect of R.F.'s history is particularly concerning vis-à-vis Dr. Oppenheimer's impression because he separately noted that the fact of a second, questionably viral-related episode, affected his thinking regarding causation. (Ex. 2, p. 3.) Moreover, in asserting an immune basis for R.F.'s recurring episodes, petitioners themselves otherwise attribute the episodes to viral illnesses. (ECF No. 76, pp. 35-37.) Accordingly, the fact that R.F.'s first episode was preceded not merely by vaccination, but also by a viral illness, has the potential to be highly significant in that the presence of the viral illness better conforms R.F.'s initial episode to the overall pattern of his chronic condition.[18]

Additionally, Dr. Oppenheimer's documented reasoning is limited and nothing in Dr. Oppenheimer's record confirms, for example, that he applied the same reasoning as Dr. Durvasula in reaching his conclusion as to the initial episode. While petitioners stress that it is not the role of treating physicians to theorize, the limits of Dr. Oppenheimer's assessment remain the limits of his assessment. The fact that Dr. Oppenheimer did not fully discuss his reasoning is not a basis for speculating that his reasoning therefore dovetails with that of Dr. Durvasula. In particular, Dr. Oppenheimer

[17] As noted in the fact summary above, there are no medical records confirming this reported treatment with antibiotics, which is concerning. However, nothing in the medical records *contradicts* the contemporaneous report of an upper respiratory infection occurring during the week prior to R.F.'s December 5, 2014 episode. And, even if the single reference to prior antibiotic treatment were somehow in error, there is at least one other contemporaneous report of a recent upper respiratory infection. (Ex. 5, p. 23.) In their briefs, petitioners acknowledge these histories without challenging them. (ECF No. 76, p. 8.)

[18] Conversely, Dr. Gans raises the separate issue that petitioners' subsequent reports to R.F.'s treating physicians appear to suggest in the longer run that R.F.'s episodes may not be related to a viral trigger, casting at least some doubt on the idea of there being any immunologic basis for the episodes. (Ex. C, p. 2 (citing Ex. 5, pp. 17-19; Ex. 29, p. 32).)

did not specify what type of immune reaction he felt explained R.F.'s initial presentation. In fact, Dr. Oppenheimer's notation disclaiming an allergic response could potentially suggest he would disagree that a hypersensitivity response is implicated as the explanation for R.F.'s initial episode.[19] In subsequent encounters, petitioners reported to other physicians that Dr. Oppenheimer had assessed a "hyper-immune response" to vaccination. (Ex. 6, p. 32; Ex. 4, p. 6.) Notably, however, when R.F. was subsequently seen by a different immunologist, that immunologist, Dr. Shimamoto, expressed that he did not understand what Dr. Oppenheimer meant by "hyper-immune response." (Ex. 4, p. 6.) Even after Dr. Shimamoto confirmed in an addendum that he was able to review Dr. Oppenheimer's record, he still characterized Dr. Oppenheimer's encounter as having provided "no definitive diagnosis." (*Id*.)

In any event, even if Dr. Oppenheimer's assessment was compelling with respect to R.F.'s initial episode, it does not support petitioners' broader claim with respect to R.F.'s chronic course. Dr. Oppenheimer felt it was only "questionable" whether R.F.'s second episode was triggered by his viral infection and specifically noted that "it would be nice to know" (*i.e.,* we do not know) what potential triggers cause R.F.'s episodes. (Ex. 2, p. 3.) Additionally, nothing in Dr. Oppenheimer's assessment reflects any hint that he believed R.F. was experiencing an autoimmune process as Dr. Durvasula has opined. In particular, Dr. Oppenheimer declined to pursue any testing even though there is testing that can speak to whether autoimmunity may be occurring. Instead, he stressed that R.F.'s differential diagnosis remained "protean," (*Id.*) which I interpret to mean varied and/or unsettled. Finally, nothing in Dr. Oppenheimer's record indicates that he believes R.F.'s initial episode was the *cause* of his chronic condition, as Dr. Durvasula opines, rather than simply being a *manifestation* of his chronic condition, as Dr. Gans opines. On the whole, Dr. Oppenheimer's record is ambiguous in that respect.

Turning then to Dr. Siegel's later primary care record, he reports as of July 19, 2017, an impression of "immune hypersensitivity reaction by mechanism – pt with very rare immune reaction seems to have been triggered by Hep B vaccine." (Ex. 6, p. 32.) He further explains, however, that R.F. had a prior "extensive work up" and "was seen by very experienced immunologist in NYC who felt he was having a hyper immune reaction which was turned on and would cont[inue] to be triggered whenever his immune system is challenged." (*Id*.) For his part, Dr. Siegel indicates that "no

[19] An "allergic reaction" is defined, simply, as a "hypersensitivity r[eaction]; used particularly to denote a type I hypersensitivity r[eaction]," and "hypersensitivity reaction" is defined as "a reaction in which the body mounts an exaggerated or inappropriate immune response to a substance either foreign or perceived as foreign, resulting in local or general tissue damage." *Allergic Reaction,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=102313&searchterm=allergic+reaction (last visited July 30, 2024); *Hypersensitivity Reaction,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=102386 (last visited July 30, 2024). Therefore, while "allergic reaction" most often refers to type-I, *i.e.,* immediate, hypertensive response, it can also be used to refer to any of the hypersensitivity reaction types. As discussed under *Althen* prong one, above, Dr. Durvasula discussed both immediate and delayed hypersensitivity without specifying which type of reaction he felt was at issue.

treatment plan [is] offered" and he "discussed [that petitioners] will get another opinion in town on dx [*i.e.,* diagnosis] and management." (*Id*.) Considering Dr. Siegel's record holistically, and especially given his recommendation that petitioners seek a diagnostic opinion elsewhere, I agree with respondent that this record is better interpreted as mere acceptance of Dr. Oppenheimer's prior evaluation than any independent assessment of vaccine causation. (ECF No. 81, p. 32.) I do acknowledge that Dr. Siegel's assessment did indicate "hypersensitivity reaction by mechanism" while separately describing Dr. Oppenheimer's prior assessment more generically as a "hyper immune reaction." (Ex. 6, p. 32.) As discussed above, Dr. Oppenheimer did not actually assess a hypersensitivity response specifically. However, to the extent one could therefore interpret Dr. Siegel as having independently assessed hypersensitivity as the operative mechanism, the remoteness of his evaluation and his lack of specialization as an immunologist reduce the value of such an assessment. *See Nuttall v. Sec'y of Health & Human Servs.,* 122 Fed. Cl. 821, 832-33 (2015) (finding that a treating physician who "only saw the patient after the injury," is not entitled to the same amount of weight as a treating physician "who had observed the patient as the condition unfolded.")

When petitioners did follow up with a new immunologist at Dr. Siegel's suggestion, Dr. Shimamoto assessed R.F. as having a "disorder involving the immune mechanism – unspecified" and expressed that it is "unclear" why he is having his repeated spells. (Ex. 4, pp. 4, 6.) Dr. Shimamoto recommended evaluating R.F.'s infant immunization series to see if there is any pattern fitting a specific immune related disease, but otherwise suggested that further specialist evaluation in pediatric immune deficiencies would be necessary. (*Id.* at 6.) Dr. Shimamoto's assessment is more consistent with Dr. Gans's opinion than it is with Dr. Durvasula's. That is, Dr. Shimamoto indicates that, while R.F. likely has an ongoing unidentified immune disorder, the reason(s) for his repeated episodes (which would include the first, allegedly vaccine-caused episode) remain unestablished.

In light of all of this, and considering the record as a whole, the medical records are not entirely devoid of medical opinion at least partly supportive petitioners' claim; however, treating physician opinion does not reliably or preponderantly support petitioners' claim without more.

ii. Expert opinions

Dr. Durvasula's opinion is short on explanation of the initial immune response at issue, which cannot be blamed entirely on the limits of R.F.'s clinical workup. At various points he indicates that it "resembled a picture of septic shock," constituted an "exaggerated immune response," was a "clear systemic inflammatory response," was a "severely exaggerated immune cascade," was a "hyperimmune response," constituted a hypersensitivity reaction, either immediate or delayed, and had clinical features of SIRS. (Ex. 22, p. 4; Ex. 27, p. 1; Ex. 30, p. 4.) Dr. Durvasula's reports are imprecise in seeming to use these terms interchangeably. As Dr. Shimamoto suggested in his review of Dr. Oppenheimer's evaluation, it is not clear whether "hyperimmune response" has any specific pathophysiologic meaning. (Ex. 4, p. 6.) And, as noted under *Althen*

prong one, Dr. Durvasula acknowledges that there are different mechanisms of hypersensitivity, though he does not specify which he is invoking. (*See* Ex. 30, p. 4.) Dr. Durvasula expressed agreement that the condition was neither anaphylaxis nor an allergic reaction, but otherwise indicated that "[t]he biological basis of such reactions is not part of clinical evaluation . . ." (Ex. 22, p. 4; Ex. 27, p. 2.) Thus, his overall conclusion is limited to characterizing R.F.'s initial episode as a "clinical syndrome" having an "immunologic nature." (Ex. 30, p. 2.) Though Dr. Durvasula suggests hypersensitivity and SIRS may overlap clinically (Ex. 30, p. 4.), Dr. Gans further explains that the two conditions are distinct. (*See* Ex. C, pp. 2-3.) Dr. Gans asserts that R.F.'s initial presentation is not consistent with either hypersensitivity or SIRS, explaining that neither condition is likely to self-resolve within hours as R.F.'s episode did. (Ex. A, p. 5.) Dr. Durvasula has not effectively addressed that point in his responsive reports.

Additionally, it should be noted that Dr. Durvasula mischaracterizes the difference of opinion between himself and Dr. Gans regarding R.F.'s more chronic course. Specifically, he asserts of Dr. Gans's opinion:

> An unnamed and unspecified chronic disorder cannot be used as a basis for rebuttal of this claim. There is no causal evidence for this argument and it is simply a refusal to acknowledge the prospect of vaccine-induced hyperimmune responses without offering an etiology. Furthermore, there is a clear association between onset of R.F.'s symptom complex and hepatitis B vaccination. No symptoms were noted prior to administration of vaccines.

(Ex. 30, p. 3.) However, the issue in this case is *not* whether the presence of an unspecified chronic condition rebuts Dr. Durvasula's opinion.

As discussed above, while Dr. Durvasula does posit a mechanism of hypersensitivity with respect to R.F.'s initial post-vaccination episode, petitioners' claim hinges on the relationship between that episode and R.F.'s more chronic, episodic presentation. In that regard, Dr. Durvasula has based his opinion on the concept of autoimmunity without identifying any actual autoimmune condition that can explain R.F.'s presentation. Thus, Dr. Gans and Dr. Durvasula are actually in agreement that R.F. suffers an unnamed and unspecified chronic disorder and Dr. Durvasula relies on the presence of such a disorder to the same extent as Dr. Gans. Where the experts differ is instead only with regard to the relationship between R.F.'s initial episode and his chronic condition.

Without knowing what the chronic condition actually is, it is speculative to reach any conclusion one way or the other as to whether the initial episode was the cause of that condition, as Dr. Durvasula opines, or merely a manifestation of the condition, as Dr. Gans opines. This remains true regardless of the fact that Dr. Durvasula purports to identify the chronic condition as being an immune condition of some kind. As discussed under *Althen* prong one, Dr. Durvasula acknowledged that "[e]xtensive immunologic and allergy testing failed to reveal a clear abnormality, immunosuppressive illness or

associated disorder of cellular or humoral immunity." (Ex. 22, p. 3.) Thus, Dr. Gans persuasively charges that Dr. Durvasula's position is unsupported. As Dr. Gans explains "while Dr. Durvasula's report is a thorough account of R.F.'s records, it is devoid of specific causal connections between the cited vaccine responses and R.F.'s condition. Additionally, plausible biologic evidence for an episodic reaction to different infectious stimuli has not been presented." (Ex. A, p. 6.)

Because petitioners bear the initial burden of proof, these limitations are detrimental to their claim, even as respondent effectively acknowledges that given the limits of R.F.'s clinical evaluations no other definitive explanation is available. While Dr. Durvasula portrays his own opinion has having a firmer grounding in the clinical history as compared to Dr. Gans's assessment, the above quotation from Dr. Durvasula's report reveals that he bases his opinion on temporal association alone, which does not support petitioners' burden of proof. *Grant,* 956 F.2d at 1148. Given that Dr. Durvasula's opinion is speculative and that petitioners bear the initial burden of proof, the fact that Dr. Gans likewise recognizes R.F.'s condition to be unidentified does not bolster petitioners' claim. Moreover, like Dr. Oppenheimer, Dr. Durvasula does not adequately account for the fact that R.F. was reportedly suffering an upper respiratory infection during the week leading up to his vaccination. (*See* Ex. 22, p. 3 (describing R.F.'s history without reference to the upper respiratory infection).) Especially in light of the assertion that subsequent similar episodes were brought on by viral illnesses, this dramatically undercuts the purported significance of the temporal relationship to the vaccination.

For all the reasons discussed above, petitioners have not met their preponderant burden of proof with respect to *Althen* prong two.

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *mot. for recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd*, 503 F. App'x. 952 (Fed. Cir. 2013); *Koehn ex rel. Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

As discussed in the factual history above, R.F. received his second hepatitis B vaccine on December 4, 2014, and he then suffered his first episode, which petitioners allege is a hypersensitivity reaction resembling SIRS, in the afternoon on the following day. (Ex. 5, p. 14; Ex. 3.) Petitioners have not substantiated that this timing of onset is

medically appropriate on this record. Petitioners cite the opinions of respondent's experts in the prior *Ahlum* case (ECF No. 82, pp. 14-15 (citing *Ahlum ex rel. TA v. Sec'y of Health & Human Servs.,* No. 12-763V, 2018 WL 4323623, at *38-39 (August 16, 2018)); however, these opinions are not actually a part of the record of this case. On this record, Dr. Durvasula does not actually identify an appropriate period of onset. To the extent petitioners urge the same mechanism as discussed in the Beretta, et al., case report, I do not see how the timing of onset of that vasculitis case is readily comparable to the clinical history in this case.

For all these reasons, petitioners have not met their preponderant burden of proof with respect to *Althen* prong three. But in any event, even if accepting that the timing of onset in this case did have the potential to implicate R.F.'s hepatitis B vaccine as a cause of his initial episode occurring one day later, petitioners' satisfaction of *Althen* prong three would not allow them to prevail given their failure to meet their burden of proof under either *Althen* prong one or two. *Althen,* 418 F.3d at 1278; *see also Grant,* 956 F.2d at 1148.

d. This is not a close case

I am mindful that the Federal Circuit has suggested that this program represents a "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280. In that regard, I acknowledge that there are aspects of this case that at first blush appear compelling. R.F., as a minor child, received a routine vaccination and the next day suffered a frightening episode. Especially in the absence of a better explanation, his treating physicians initially felt the circumstances potentially implicated his vaccination. In hindsight, even though this first episode resolved, it marked a turning point in R.F.'s health and his condition remains enigmatic, though even the government's expert agrees he has an ongoing chronic disorder of some kind that is being episodically triggered. Ultimately, however, this is not a close case despite these circumstances.

The Vaccine Act only relaxes proof of causation for Table Injuries only. *Grant*, 956 F.2d at 1147-48. A cause-in-fact claim requires petitioner to do the "heavy lifting" of affirmatively proving by preponderant evidence that R.F.'s vaccination was the cause of his injury. *Hodges v. Sec'y of Health & Human Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993) (indicating that in the absence of a Table Injury, "the heavy lifting [of proving causation] must be done by the petitioner, and it is heavy indeed"); *see also Althen*, 418 F.3d at 1280 (clarifying that "heavy lifting" characterizes the preponderant evidence standard and not any heightened burden of proof.) Temporality alone does not establish causation-in-fact. *Grant*, 996 F.2d at 1148.

Here, petitioners were unpersuasive in seeking to explain R.F.'s chronic course as an unspecified autoimmune condition. Thus, even if R.F.'s initial episode was vaccine related, the relationship between R.F.'s various episodes, and the relationship between each episode and his unidentified underlying condition, would still remain entirely unclear. And, although petitioners contend that the chronicity of R.F.'s

unspecified underlying condition has separately resulted in osteopenia, they have not identified any condition that marries these two aspects of R.F.'s clinical history as part of any known clinical presentation. Thus, they have not demonstrated that the individual episodes of hypothermia/hypotonia are the cause of that osteopenia, have a cumulative effect, or otherwise change the course of the underlying condition. Because petitioners bear the initial burden of proof, all of these issues are detrimental to their case.

Petitioners contend that their proposed explanation of events is more likely than the idea that onset of R.F.'s condition was merely coincident to vaccination. (ECF No. 76, p. 37.) However, for all the reasons discussed above, this decision does not turn on the notion of coincidence. Even if one were to find R.F.'s hepatitis B vaccine compelling as a potential trigger of his first episode, this does not lead invariably to the conclusion that a compensable injury has occurred. Petitioners themselves theorize that each of R.F.'s episodes have a separate trigger. In that vein Dr. Gans has further explained on respondent's behalf that R.F.'s post-vaccination episode can be a *manifestation* of his underlying immune disorder without being a *cause* of the underlying condition. This reasoning applies regardless of whether R.F.'s vaccination is implicated as a trigger of that single episode. Standing alone, R.F.'s initial episode alone does not meet the Vaccine Act's severity requirement.

VII. Conclusion

R.F. has clearly suffered and for that he and his family have my sympathy. However, for all the reasons discussed above, petitioners have not demonstrated by preponderant evidence that his condition was caused by his vaccination. Accordingly, this case is dismissed.[20]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[20] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.